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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/674,702	09/30/2003	Gail K. Buehler	MCP5017	4561

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EXAMINER	
SOROUSH, LAYLA	

ART UNIT	PAPER NUMBER
1627	

NOTIFICATION DATE	DELIVERY MODE
05/12/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/674,702	BUEHLER ET AL.	
	Examiner	Art Unit	
	LAYLA SOROUSH	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8-19 and 21-25* is/are pending in the application.

4a) Of the above claim(s) *18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-17,19 and 21-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 22, 2010. Claims 1-6, 8-17, 19, 21-25 are pending.

The following rejections are made:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6, 8-17, 19, 21-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gowan, Jr. (US 5374659 A—previously presented), Gergely et al. (US 5834019 A – previously presented), Patel et al. (US Pat No. 6569463), Eichman (US Pat. No. 5,980,882—previously presented), McNamara et al. (6423298) Hagemann et al. (US Pat 5,211,957– previously presented) and Saeedi et al. (PREVENTION OF CRYSTAL GROWTH IN ACETAMINOPHEN SUSPENSIONS BY THE USE OF POLYVINYL PYRROLIDONE BOVINE SERUM ALBUMIN; DARU Volume 11, No 3, 2003).

Gowan, Jr. teaches an aqueous pharmaceutical suspension composition comprising an insoluble pharmaceutical active, a suspension stabilizing effective amount of xanthan gum (hydrocolloid and thickener), pregelatinized starch (swelling agent and thickener) and polyoxyethylene sorbitan monooleate (surfactant) (see abstact). The pH of the composition is preferably between 3.5 and 5 (col 5 line 6). Application of the compositions and method of the present invention for medical and pharmaceutical uses can be accomplished by any clinical, medical and pharmaceutical methods and techniques as are presently or prospectively known to those skilled in the art. Thus it is intended that the present invention cover the modifications and variations of this invention provided that they come within the scope of the appended claims and their equivalents (col 7 lines 54-61).

The reference fails to teach the active agent- Loratadine, the nucleation inhibitor - PVP, and the amino polycarboxylic acid compound- EDTA.

Gergely et al. is solely used to show that Loratadine is virtually completely water-insoluble and has a very strongly hydrophobic character. It is thus extremely poorly wettable and therefore difficult to suspend. Its fine particles furthermore have the tendency to form a film on the water surface, to creep up the glass wall to a pronounced extent and to adhere relatively strongly there.

Patel et al. teaches "compositions of the present invention can be used for improved delivery of hydrophilic or hydrophobic pharmaceutical active ingredients, such as drugs, nutritional, cosmeceuticals and diagnostic agents (Col 28 line 57-67)." Such pharmaceuticals include loratadine. The

pharmaceutical compositions can include one or more additive such as **solubilizers**, i.e., additives to increase the solubility of the pharmaceutical active ingredient (col 29 lines 16-21). The "solid pharmaceutical compositions of the present invention can optionally include one or more additives, sometimes referred to as excipients. The additives can be contained in an encapsulation coat in compositions which include an encapsulation coat, or can be part of the solid carrier, such as coated to an encapsulation coat, or contained within the components forming the solid carrier. Alternatively, the additives can be contained in the pharmaceutical composition but not part of the solid carrier itself (col 28 lines 57-67)." Hence reading on the limitation uniformly dispersed nucleation inhibitor of claim 1. Preferred **solubilizers** for use in the compositions include triacetin, triethylcitrate, ethyl oleate, ethyl caprylate, dimethylacetamide, N-methylpyrrolidone, N-hydroxyethylpyrrolidone, polyvinylpyrrolidone(nucleation inhibitor) (Col 29 line 57-60). Other additives include enzyme inhibitors and chelating agents such as EDTA.

Additionally, Patel et al. teaches "Spherical particles are preferred, and these may be produced through spheronization or a spherical crystallization process. Crystals or compact granules from dry compaction or extrusion processes, often available commercially, serve as good substrates (col 41 lines 5-10)."

Eichman teaches drug resin complexes stabilized by chelating agents. "The particle size of a resin can differ between two resins." The chelating agent

is preferably EDTA (amino polycarboxylic acid compound). EDTA is known to stabilize drugs in solution by retarding their oxidation col 2 lines 60-61).

McNamara et al. teaches EDTA is used to improve long term storage, surfactants, and suspension stabilizing agents.

Hagemann et al. teaches pharmaceutically acceptable excipients including PVP are, in particular viscosity index improvers which are suitable for stabilizing aqueous suspensions and which inhibit sedimentation (col 4 lines 42-65).

It would have been obvious to one of ordinary skill in the art to combine the teachings of Gowan, Jr., Gergely et al., Patel et al., Eichman, and Hagemann et al. The motivation to combine the teachings is because (1) Gowan, Jr. teaches an aqueous pharmaceutical suspension composition comprising an insoluble pharmaceutical active, a suspension stabilizing effective amount of xanthan gum (hydrocolloid and thickener), pregelatinized starch (swelling agent and thickener) and polyoxyethylene sorbitan monooleate (surfactant) (see abstact). Application of the compositions and method of the present invention for medical and pharmaceutical uses can be accomplished by any clinical, medical and pharmaceutical methods and techniques as are presently or prospectively known to those skilled in the art. Thus it is intended that the present invention cover the modifications and variations of this invention provided that they come within the scope of the appended claims and their equivalents (col 7 lines 54-61); (2) Gergely et al. teaches Loratadine is virtually completely water-insoluble and has a very strongly hydrophobic character. It is thus extremely poorly wettable and therefore difficult to suspend. Its fine particles furthermore have the tendency to

form a film on the water surface, to creep up the glass wall to a pronounced extent and to adhere relatively strongly there., (3) Patel et al., teaches solubilizers for use in the compositions include triacetin, triethylcitrate, ethyl oleate, ethyl caprylate, dimethylacetamide, N-methylpyrrolidone, N-hydroxyethylpyrrolidone, polyvinylpyrrolidone(nucleation inhibitor) (Col 29 line 57-60). Other additives include enzyme inhibitors and chelating agents such as EDTA (4) Eichman teaches drug resin complexes stabilized by chelating agents. "The particle size of a resin can differ between two resins." The chelating agent is preferably EDTA (amino polycarboxylic acid compound). EDTA is known to stabilize drugs in solution by retarding their oxidation col 2 lines 60-61) and (5) Hagemann et al. teaches pharmaceutically acceptable excipients are, in particular viscosity index improvers which are suitable for stablising aqueous suspensions and which inhibit sedimentation include PVP (col 4 lines 42-65). A skilled artisan would have reasonable expectation of effectively stabilizing loratadine (antihistamine) a water-insoluble pharmaceutical active.

Gowan, Jr., Gergely et al., Patel et al., and Eichman meet all elemental steps of the instant claims and the compositions created thereof. Since the compositions prepared by Gowan, Jr., Gergely et al., Patel et al., and Eichman meets all elemental components of the instantly prepared composition, they would obviously exhibit the same properties as recited in claims 8-10 and 22. Although the reference teaches within the embodiment of the invention crystalline drug forms are envisaged, whether the drug is in crystal form or

amorphous form does not effect the composition. Hence, the various forms are rendered obvious by the teachings of the prior art.

Claims 1-6, 8-17, 19, 21-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reinhardt et al. (US Pat No. 6,217,998) in view of Hansenne et al. (US Pat No. 6916464 B2),Walch (US Pat No. 6790847), and Patel et al. (US Pat No. 6569463).

Reinhardt et al. teaches a composition comprising EDTA, xanthan gum, PVP, fillers, and pigments. Prior to application to the sponge the composition of Reinhardt et al. is an aqueous suspension.

The reference fails to teach the pH claimed or the active agent loratadine in crystal form.

Hansenne et al. is solely used for the teaching that "When the physiologically acceptable medium is an aqueous medium, it generally preferably has a pH which is compatible with the skin preferably ranging from 3 to 9 and better still from 3.5 to 7.5."

Walch teaches a drug composition useful for topical application of antihistamines loratadine which are incorporated with cosmetics and pigments (col 5 lines 5-8).

Patel et al. teaches "compositions of the present invention can be used for improved delivery of hydrophilic or hydrophobic pharmaceutical active ingredients, such as drugs, nutritional, cosmeceuticals and diagnostic agents (Col 28 line 57-67)." Such pharmaceuticals include loratadine. The

pharmaceutical compositions can include one or more additive such as **solubilizers**, i.e., additives to increase the solubility of the pharmaceutical active ingredient (col 29 lines 16-21). The "solid pharmaceutical compositions of the present invention can optionally include one or more additives, sometimes referred to as excipients. The additives can be contained in an encapsulation coat in compositions which include an encapsulation coat, or can be part of the solid carrier, such as coated to an encapsulation coat, or contained within the components forming the solid carrier. Alternatively, the additives can be contained in the pharmaceutical composition but not part of the solid carrier itself (col 28 lines 57-67)." Hence reading on the limitation uniformly dispersed nucleation inhibitor of claim 1. Preferred **solubilizers** for use in the compositions include triacetin, triethylcitrate, ethyl oleate, ethyl caprylate, dimethylacetamide, N-methylpyrrolidone, N-hydroxyethylpyrrolidone, polyvinylpyrrolidone(nucleation inhibitor) (Col 29 line 57-60). Other additives include enzyme inhibitors and chelating agents such as EDTA. The compositions can be formulated for oral, nasal, buccal, ocular, urethral, transmucosal, vaginal, topical or rectal delivery. Additionally, Patel et al. teaches "Spherical particles are preferred, and these may be produced through spheronization or a spherical crystallization process. Crystals or compact granules from dry compaction or extrusion processes, often available commercially, serve as good substrates (col 41 lines 5-10)."

Therefore, a skilled artisan would have reasonable expectation of successfully producing a topical formulation with a local antihistamine effect with the pH claimed. The motivation comes from the teaching of Walch that the

antihistamine loratadine is useful for topical application; the composition is incorporated with cosmetics inclusive of pigments; and Hansenne et al. it is generally preferably has a pH which is compatible with the skin preferably ranging from 3 to 9 and better still from 3.5 to 7.5. Hence, a skilled artisan would have had reasonable expectation of successfully producing a composition with similar efficacy and results.

Response to Arguments

Applicant's arguments filed March 22, 2010 have been fully considered.

Applicant argues the prior art does not teach the EDTA is useful in imparting pH and viscosity stability. The Examiner maintains position that EDTA is generally known to stabilize drugs in solution by retarding their oxidation as shown by Eichman (col 2 lines 60-61). McNamara et al. teaches EDTA is used to improve long term storage, surfactants, and suspension stabilizing agents.

Additionally, with respect to the argument that the nucleation inhibitor prevents the growth of particles, the Examiner states Hagemann et al. teaches pharmaceutically acceptable excipients including PVP are, in particular viscosity index improvers which are suitable for stabilizing aqueous suspensions and which inhibit sedimentation (col 4 lines 42-65). Also, Saeedi teaches PVP showed interesting results regarding sedimentation volume, resuspendability, prevention of cake formation, and crystal growth inhibition; and offer new perspectives in the preparation of suspensions.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Layla Soroush whose telephone number is (571)272-5008. The examiner can normally be reached on Monday through Friday from 8:30 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shengjun Wang/
Primary Examiner, Art Unit 1627